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VIEWPOINT

If Only Cardiologists Did Properly Measure Blood Pressure

Blood Pressure Recordings in Daily Practice and Clinical Trials

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Blood pressure (BP) is often measured sloppily, not only in clinical practice, where seemingly more important cardiovascular information, such as ejection fraction, cardiac output, and wedge pressure, is available, but also in clinical trials. Yet, definite conclusions often hinge on accurate BP measurements. In the Heart Outcomes Prevention Evaluation (HOPE) study, the conclusion of the benefits being relatively independent of BP was challenged by 24-h ambulatory BP monitoring in a subgroup that documented a larger fall in BP than reported in the whole population. Whether measured in office or clinical trials, BP is an important clinical tool that should be treasured by practitioners and clinical investigators alike. (J Am Coll Cardiol 2002;40:2201–3) © 2002 by the American College of Cardiology Foundation

"The measurement of blood pressure is likely the clinical procedure of greatest importance that is performed in the sloppiest manner" (1). Blood pressure (BP) is an extremely labile hemodynamic parameter; it varies from heartbeat to heartbeat, from morning to evening, from winter to summer, from sleeping to awake, and from sitting to standing. The same holds true, however, for any other cardiovascular hemodynamic parameter, such as heart rate, cardiac output, ejection fraction, or pulmonary wedge pressure. Information that is based on more invasively obtained hemodynamic measurements is often considered more pertinent than information based on a simple BP recording. Many of our colleagues have become somewhat nonchalant about taking BP, particularly when extensive and seemingly more meaningful hemodynamic information is available, as is often the case for cardiologists. In a survey of 114 participants, not a single physician completely followed all the techniques of BP measuring that were recommended by the American Heart Association (2). Yet, numerous studies have documented that BP measured carefully under standardized conditions in the physician's office (3) is one of the most powerful and reliable prognosticators available.

Nonchalance or, to use Kaplan's less euphemistic term, sloppiness in taking BP is not only encountered in daily practice, but also in large randomized, prospective trials in patients with coronary heart disease, congestive heart failure, and, *horribile dictu*, even in studies on hypertension. Not uncommonly in these trials, BP data are not available at all, were taken at random in a nonstandardized way, or, even worse, were referred to as presence or absence of a history of hypertension. In the Prospective Randomized Evaluation of the Vascular Effects of Norvasc Trial (PREVENT) (4) and the Quinapril Ischemic Event Trial (QUIET) (5), both of which compared antihypertensive drugs (amlodipine or quinapril, respectively) against placebo in patients with coronary artery disease, information regarding BP is either lacking or insufficient, making interpretation of the findings very difficult. Even in some studies in which outcome hinged on lowering BP with antihypertensive therapy, patients in whom BP data were missing altogether were diagnosed as having hypertension "by other criteria" (6). Yet, most often when these studies are analyzed, the question as to the effect of the cardiovascular drug on BP suddenly becomes increasingly important. Even small differences in BP that seem to have little clinical significance can translate into impressive morbidity and mortality benefits. In the Swedish Trial in Old Patients with Hypertension (STOP) study, a 4-mm decrease in diastolic pressure led to a 50% reduction of cardiovascular events in diabetic hypertensive patients (7).

Even more to the point is the Heart Outcomes Prevention Evaluation (HOPE) trial (8,9), which must be considered a landmark study attesting to the efficacy of angiotensin-converting enzyme (ACE) inhibitors in reducing cardiovascular events in patients with vascular disease. Yet, in the HOPE study, information pertaining to BP measuring is rather meager. The authors merely state in the discussion part of the paper: "We assessed blood pressure by cuff pressures, which is the normal approach in clinical practice…" (8). Because the difference between patients on ramipril and those on placebo was only 3/2 mm Hg, the authors, on the basis of these BP measurements, thought that the impressive benefits observed were chiefly the result of ACE inhibitor therapy and less related to the fall in BP. Indeed, in the accompanying editorial, Francis (10) appropriately stated that ACE inhibitors "appear to have effects on the vasculature, heart, and kidneys that go far beyond their rather small blood pressure-lowering effects." More recently, Yusuf (11) noted that the "HOPE's 32% reduction in strokes was three times that expected by blood pressure alone."

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Abbreviations and Acronyms

ACE	= angiotensin-converting enzyme
BP	= blood pressure
HOPE	= Heart Outcomes Prevention Evaluation
PREVENT	= Prospective Randomized Evaluation of the Vascular Effects of Norvasc Trial
QUIET	= Quinapril Ischemic Event Trial
Syst-Eur	= Systolic Hypertension in Europe

Recent data on 24-h ambulatory BP monitoring in the HOPE study challenge this view. In a subset of patients who underwent ambulatory 24-h BP monitoring, Svensson et al. (12) documented a significant decrease in systolic and diastolic pressure with ramipril when compared with placebo, greatly exceeding the values hitherto reported in the HOPE study. Although ramipril did not significantly reduce clinic BP, average 24-h ambulatory BP was reduced by 10/4 mm Hg ($p < 0.03$), and this reduction was distinctly more pronounced during the nighttime by 17/8 mm Hg ($p < 0.001$) (Fig. 1). Because ramipril was dosed in the evening, it is not surprising that the greatest difference in BP occurred during the nighttime, and the antihypertensive effect was weakening progressively throughout the day, at the time it was measured in the physician's office.

In the Systolic Hypertension in Europe (Syst-Eur) study, ambulatory systolic BP was a better predictor of cardiovascular risk than was conventional BP (13). In fact, nighttime systolic BP most strongly predicted cardiovascular mortality, all cardiovascular end points, and fatal and nonfatal stroke (13). Similarly, Verdecchia et al. (14,15) reported in more than 1,100 patients followed for up to seven years that ambulatory BP stratified cardiovascular risk independent of clinical BP. One might argue that the small subset of patients in the study of Svenson et al. (12) may not have been representative for the whole population in the HOPE study. However, even if this were the case, most if not all HOPE results could be explained by the reported reduction in BP (16), and there is little reason to invoke ancillary (nonhemodynamic) properties of ACE inhibitors in general or ramipril in particular. Indeed, even the authors of the substudy admitted "the effects on cardiovascular morbidity and mortality seen with ramipril in the HOPE study may, to a larger extent than previously ascribed, relate to the effects on blood pressure patterns over a 24-h period."

Of note, the fact that the impressive benefits of an ACE inhibitor in the HOPE trial were (at least to some extent) mediated by the fall in BP should not by any means diminish the status of the HOPE study as a landmark trial.

Two lessons remain to be learned:

1. Blood pressure should be measured in a rigorous and standardized way in all trials of cardiovascular drugs, even in those trials not designed to primarily assess antihypertensive efficacy. Additionally, 24-h ambulatory BP monitoring should be done in a representative subsample of the study population.
2. Blood pressure, when measured carefully in the physician's office, remains one of the most powerful and most accurate determinants of cardiovascular status and future cardiovascular events. The mere fact that BP measurements are inexpensive, easily obtainable, and noninvasive should not diminish their clinical importance. Clearly, this simple clinical tool should be respected and treasured by investigators in clinical trials and all practicing physicians alike.

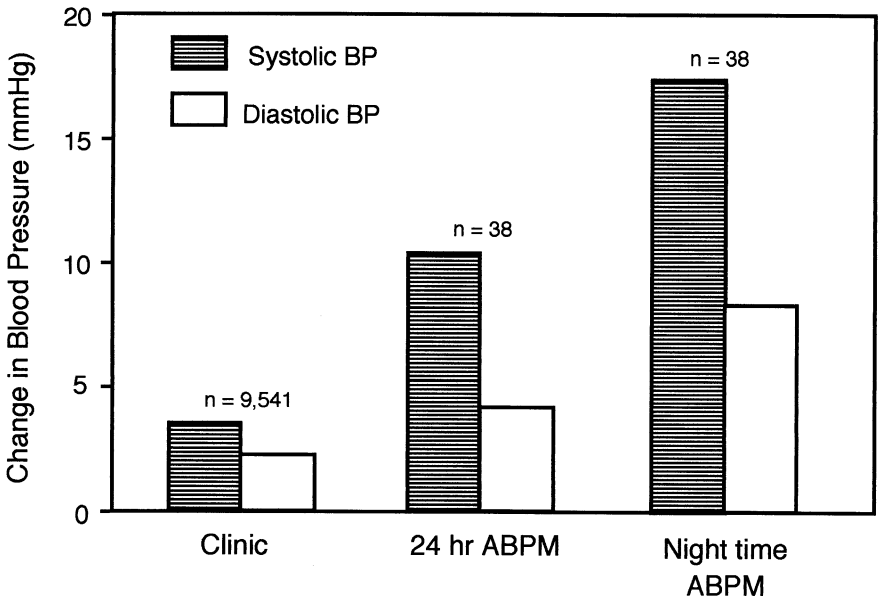

Figure 1. Comparison of cuff blood pressure (BP), 24-h ambulatory BP (ABPM) and nighttime ambulatory BP in the Heart Outcomes Prevention Evaluation (HOPE) study and in a HOPE substudy.

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REFERENCES

1. Kaplan NM. Commentary on the sixth report of the Joint National Committee (JNC-6). Am J Hypertens 1998;11:134–6.
2. McKay DW, Campbell NRC, Parab LS, Chockalingam A, Fodor JG. Clinical assessment of blood pressure. J Hum Hypertens 1990;4:639–45.
3. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med 1997;157:2413–46.
4. Pitt B, Byington RP, Furberg CD, et al. Effect of amlodipine on the progression of atherosclerosis and the occurrence of clinical events. PREVENT Investigators. Circulation 2000;102:1503–10.
5. Pitt B, O'Neill B, Feldman R, et al. The QUinapril Ischemic Event Trial (QUIET): evaluation of chronic ACE inhibitor therapy in patients with ischemic heart disease and preserved left ventricular function. Am J Cardiol 2001;87:1058–63.
6. Pahor M, Guralnik JM, Corti MC, Foley DJ, Carbonin P, Havlik RJ. Long-term survival and use of antihypertensive medications in older persons. J Am Geriatr Soc 1995;43:1191–7.
7. Hansson L. First-line antihypertensive therapy (letter). Lancet 2000; 356:508–9.
8. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000;355:253–9.
9. Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342:145–53.
10. Francis GS. ACE inhibition in cardiovascular disease. N Engl J Med 2000;342:201–2.
11. Yusuf S (as reported by Alexander W). ACE/AII combo tested on endothelial dysfunction. Cardiol Today 2001;4:6.
12. Svensson P, de Faire U, Sleight P, Yusuf S, Ostergren J. Comparative effects of ramipril on ambulatory and office blood pressures: a HOPE substudy. Hypertension 2001;38:E28–32.
13. Staessen J, Thijs L, Fagard R, et al. Predicting cardiovascular risk using conventional vs. ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators. JAMA 1999;282:539–46.
14. Verdecchia P, Porcellati C, Schillaci G, et al. Ambulatory blood pressure: an independent predictor of prognosis in essential hypertension. Hypertension 1994;24:793–801.
15. Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Pede S, Porcellati C. Ambulatory pulse pressure: a potent predictor of total cardiovascular risk in hypertension. Hypertension 1998;32:983–8.
16. Staessen JA, Wang J-G, Thijs L. Cardiovascular prevention and blood pressure reduction: a meta-analysis. Lancet 2001;358:1305–15.